VL in India – maximizing the research infrastructure in India
[The role of research in the sustained elimination of VL]

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India, Nepal and Bangladesh harbour an estimated 67% of the global VL disease burden.

Endemic districts
- India: 55
- Bangladesh: 45
- Nepal: 12

Asymptomatic Leishmania infection in Community (RMRI)

Door-to-door survey of 242 households of two highly endemic villages

1048 individuals were clinically examined and subjected to rK39 and PCR

Point prevalence of Asymptomatic cases: **11.5 per 100** population

Disease conversion rate within one year: **17.36 per 100** asymptomatic cases

Asymptomatic cases need attention
National Road Map for Kala-azar Elimination - 2014

- Launched in Sept. 2014
- Activity wise Time lines defined for implementation
- State/ District / Block level TASK FORCE constituted to foresee programme activities
- Ambisome rolled out
- Development partners involvement
- Guidelines on KA elimination developed and uploaded
VL Research Infrastructure Challenges

- Diagnosis: Prevalence of asymptomatic and PKDL cases in endemic populations
- Efficacy of various active case search tools viz. camp, index, incentive, snowball approach
- Safety and efficacy assessment of newer drugs and treatment modalities through clinical trials
- Validation of Insecticide Quantification Kits (IQKs) in India for the improvement of IRS against VL vectors. (Collaborated work of RMRI & LSTM-BMGF)
- Development of Disease Data Management System (DDMS) to support NVBDCP track progress and make informed decisions

PKDL Cases in India since 2011 to 2016 (July)

<table>
<thead>
<tr>
<th>Year (July)</th>
<th>PKDL Cases</th>
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<tbody>
<tr>
<td>2011</td>
<td>841</td>
</tr>
<tr>
<td>2012</td>
<td>429</td>
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<tr>
<td>2013</td>
<td>499</td>
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<tr>
<td>2014</td>
<td>421</td>
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<tr>
<td>2015</td>
<td>648</td>
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<tr>
<td>2016</td>
<td>850</td>
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</table>
i) Early diagnosis and complete treatment with effective drugs

ii) Effective vector management

iii) Effective Information, Education and Communication (IEC) and Behavior Change Communication (BCC) for improved community participation
How RIs be strengthened for sustained elimination of VL?

A Coherent sequence of Activities

Corpus Funds for Infrastructure development & for effective VL elimination

Concept  Development  Implementation  Operation

World Class RI
For the sustained elimination of VL

Design Study
Preparatory Phase
Support to Implementation & Operation Individual projects - Clusters

Integrating Activities
Innovation & Human resources

Policy support actions – International Cooperation
Research Infrastructure strengthening VL diagnosis

Needs:
- Early diagnosis and complete treatment with minimal delay after onset of signs & symptoms
- Antigen-based rapid diagnostic tool supportive for test of cure
- Quick and reliable diagnosis of PKDL and VL-HIV co-infection and treatment at point of care
- Detection of asymptomatic cases and PKDL in disease transmission

✓ Non-invasive diagnostic method using oral fluid and urine samples
✓ Antigen-based diagnostic method (RBC-ELISA)
Diagnosis of VL

- Clinical signs and symptoms supported with RDT test is in mainstay for diagnosis of fresh VL cases.

- However, test of cure and diagnosis of relapse cases is still cumbersome.

- Antigen-based Rapid Diagnostic test (LAMP), already developed by NIOP, can be solution for the same. Needs to be implemented.

- Other potential molecules identified by at NII, RMRI and others need to be validated and developed as RDT.
Research Need in context of current scenario

Diagnosis of PKDL

- Clinical signs and symptoms supported with RDT test is in practice at periphery level.
- However, confirmatory test (microscopy) needs expertise and even though less sensitivity of microscopy in macular form is of major concern.
- Simple, sensitive, specific and feasible test at periphery level needs to be developed.

Diagnosis of VL-HIV co-infection

- Cross diagnosis of VL by RDT and HIV cases at ICTC has recently been introduced, however, low sensitivity of RDT in VL-HIV co-infection is a major concern. Research for development of highly sensitive and specific tool is required.
Research Need in context of current scenario

### Treatment Options

- Implementation of the first ever oral miltefosine for VL with almost 95% efficacy.
- Poor compliance compelled the policy makers to phase out this drug.
- Now Single dose ambisome (SDA) for VL and still miltefosine for PKDL is in the mainstay of treatment.

- Research for new drug combinations, dosage and introducing formulation - New Investigational products (IP) for treatment need to be identified and passed through phase-wise clinical trials.
- Research need for systematic pharmacovigilance and cohort monitoring of drugs in use at program level to sustain effective treatment.
Vector Control Current Scenario

Continuous decline in Kala-azar cases from 2012.....

- Two regular rounds of IRS
- Programme ownership at state & district levels
- Deployment of Man Power by GoI and partners at district & block level like VBD Consultant KTS, DEO
- Enhanced Supervision & Monitoring by NVBDCP and partners
- Regular review at Centre, State and district levels

VBD Consultants: Vector Born Disease Consultants : KTS Kala Azar Technical Supervisor
Resistance development to DDT is of major concern.

Ultimately 2-round of IRS with Synthetic pyrethroid was implemented in program at pilot level and proposed to extend in all endemic districts during 2017 IRS cycle.

However, research on insecticide rotation may be undertaken to avoid resistant development to insecticide in long use.

- Application of IQK in quality and quantity assessment of IRS
- Use of compression Pump in place of stirrup pump in IRS
- Use of DDMS to correlate impact of IRS in disease control
- Effective vector control with combined interventions (IRS+LN Permanet-3.0) as compared to any of the single method.
- Long lasting insecticidal nets as an effective, acceptable and cost-effective preventive tool
- Use of KO-Tab 123 impregnated bed nets

DDMS: Disease Data Management System; insecticide quantification kit (IQK); Indoor Residual Spraying (IRS)
Research Infrastructure Need for Monitoring & Surveillance

- Disease Surveillance: Application of Remote sensing and GIS tool in hot-spot mapping of VL: Understanding mechanism for disease migration to new areas
- Information technology: adverse reaction reporting
- Further study of sand fly biology and ecology (breeding site, longevity, flight range, etc.) in current context.
- Research into disease transmission & Mathematical Modelling for VL
- Effective tools for impact evaluation of IRS (IQK and DDMS may be applied).
- Proper identification and management of VL-HIV, VL-TB, VL-Diabetes co-infected cases
- Managing Human Resources as a Skilled Managers:
  - Training to KTS and VBD consultants for effective monitoring and supervision at peripheral level
  - Impact of ASHA training on active case detection of VL in Bihar, India (about 7-fold increase in referral by ASHAs after two-round training)

- VBD Consultants: Vector born disease consultants: KTS Kala Azar Technical Supervisor
Impact of
Visceral / Cutaneous Leishmaniasis is
Maximum in Improvised & Conflict Zones

IMPACT OF NON HEALTH SECTOR:
• Access of VL treatment through PHC clinics: increasing the reach and access through awareness and education
• Socio-economic growth in endemic areas
• Providing Proper Hygiene, and sanitation
• Environmental management by maintenance of sanitation and construction of Pucca (concrete) houses
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